

CLAIMS

1. A process for the preparation of a dispersion of nano-crystalline particles in an aqueous medium comprising combining:
  - 5 a) a first solution comprising a substantially water-insoluble substance in a water-miscible organic solvent with;
  - b) an aqueous phase comprising water and optionally a stabiliser, to form a dispersion of amorphous particles; and
  - c) sonicating the dispersion of amorphous particles for a sufficient period to form nano-  
10 crystalline particles of the substantially water-insoluble substance; and optionally removing the water-miscible organic solvent.
2. A process according to claim 1 wherein the nano-crystalline particles have a mean particle size of from 50 to 250nm.  
15
3. A process according to claim 1 or 2 wherein the substantially water-insoluble substance is a substantially water-insoluble pharmacologically active compound.
4. A process according to any one of the preceding claims wherein the concentration of substantially water-insoluble substance in the combined solution and aqueous phase following step (b) of the process is 10 mM or less.  
20
5. A process according to claim 4 wherein the concentration of substantially water-insoluble substance in the combined solution and aqueous phase following step (b) is from 0.5 to 3 mM.  
25
6. A process according to any one of the preceding claims wherein the aqueous phase contains a stabiliser.
- 30 7. A process according to claim 6 wherein the stabiliser comprises a polymeric dispersant and an amphiphilic surfactant.

- 25 -

8. A process according to claim 7 wherein the stabiliser comprises a polymeric dispersant and an anionic surfactant.
9. A process according to claim 8 wherein the polymeric dispersant is polyvinylpyrrolidone and the anionic surfactant is sodium dodecyl sulfate.
10. A process according to any one of claims 7 to 9 wherein the amphiphilic surfactant is at a concentration below the amphiphilic-polymer critical association concentration.
- 10 11. A process according to any one of the preceding claims wherein the combination of the first solution and aqueous phase is carried out with rapid mixing.
12. A process according to claim 11 wherein rapid mixing comprises sonication during the combination.
- 15 13. A process according to any one of the preceding claims wherein the combination of the first solution and the aqueous phase is carried out in less than 30 seconds.
14. A process according to any one of the preceding claims wherein the first solution is added to the aqueous phase.
- 15 15. A process according to any one of the preceding claims wherein the dispersion of amorphous particles formed following combination of the first solution and the aqueous phase is sonicated for at least 10 minutes (preferably from 20 to 100 minutes).
- 25 16. A process according to any one of the preceding claims wherein the sonication takes place at a temperature below 50°C.
17. A process according to any one of the preceding claims which further comprises isolating the nano-crystalline particles from the aqueous medium.

**BEST AVAILABLE COPY**